EPOTECH (2)

Innovation means quality

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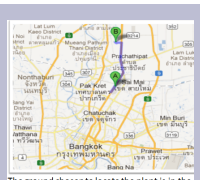
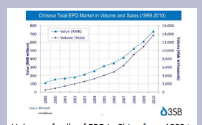
Biotechnology Degree Final Project for Universitat Autònoma de Barcelona



The ground chosen to locate the plant is in the point A and the point B shows the location of the Thailand Science Park, am important research center on Biotechnology.

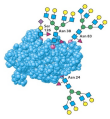
EPOTECH is an emerging biotechnological company centered on the production of biopharmaceutical products.
This project proposes the construction of a new plant in Sai Mai, 20 Km far from Bangkok (Thailand) for the production of recombinant human erythropoietin (rhEPO).
The market to be exploited is China because it is an industrially emergent country that is adopting Western habits and it makes it a potentially pharmaceutical new market. Concretely, it is estimated that there are 119.5 million of CKD (Chronical Kidney Disease) patients that need rhEPO to treat anemia. 3SBio is the company that currently distributes this product, so Epotech is planning to sell them rhEPO as an API (Active Pharmaceutical Ingredient) for a lower price than its current suppliers.



Volume of sells of EPO in China from 1999 to 2010 by 3SBio.

OBJECTIVE

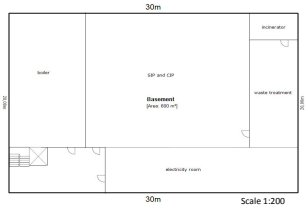
Design a production plant of rhEPO expressed on CHO cells by using a batch production system.
Analyze it's economical viability and environmental and social impact, producing in Thailand and selling in China.

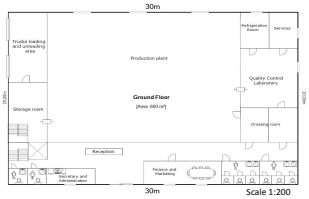


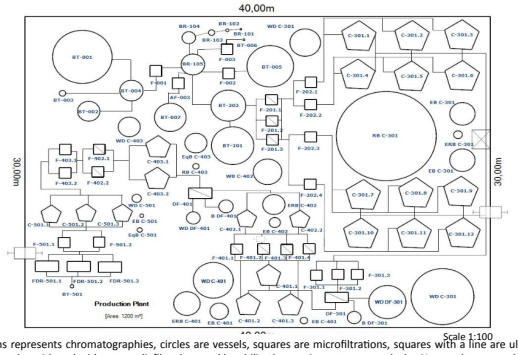
Erythropoietin (EPO) is a glycoprotein of hormonal system that regulates erythropoiesis: it stimulates the proliferation and differentiation of precursor cells of erythrocytes placed in the bone marrow.
At a molecular level, human EPO is a glycoprotein of 165 amino acids and a molecular weight of 35 KDa approximately depending on the pattern of glycosylation. It has been observed that EPO isoforms rich in sialic acids (negatively charged) at the last sugar of N-glycosilation present higher half lives.

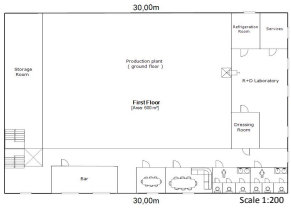
The production cell line is **rhEPO-CHO.K1** (Chinese Hamster Ovary). It was obtained from the Cell Cultures Laboratory of the Biochemistry and Biological Sciences Faculty at the Universidad Nacional del Litoral (Santa Fe, Argentina).
The operational system used is a **batch**, which eases the entrance to a new market.

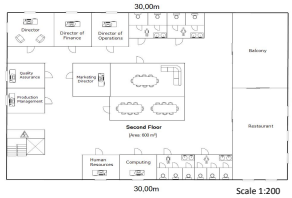
PLANT LAYOUT











Pentagons represents chromatographies, circles are vessels, squares are microfiltrations, squares with a line are ultrafiltration and rectangles with and without are diafiltrations and lyophilisation equipments, respectively. Nomenclature used is the same as EPOTECH (1) , but there are new vessels, indicated as: RB: regeneration buffer, EB: elution buffer, ERB: equilibrate and wash buffer, WD: wash disposal, EqB: equilibration buffer. *RapidSketch* software.

EPOTECH's new plant is a unique building that accomplishes good manufacturing practices (GMP): dressing rooms and autoclave systems ( ) are the only way that connect the rest of the plant with the production area. The plant layout proposed is referred to the process flow diagram described in EPOTECH (1).
In the R+D laboratory, it is produced the inoculums for the inoculation train, placed in the production plant, in a 2 L bioreactor.

SUSTAINABILITY ANALYSIS

ECONOMY

EVALUATION

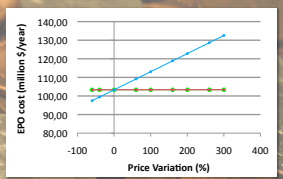
Total Capital Investment	253,736,000 $
Operating Cost	103,303,000 $/year
Revenues	3,140,000 $/year
Unit Production Cost	1,178.85 $/g
Selling price	35.83 $/g
Gross Margin	-3,190.38 %
Return On Investment (ROI)	-30.51 %
Net Present Value (NPV)	-742,165,000 $

The selling price of 3SBio, the principal potential consumer is 36 $/g.

In 15 years of the production plant lifetime the initial investment will not be recovered ➡ **This project is not economically viable.**
Reasons:

1. Inconsistent bibliographic data from fermentation process and downstream purification.
2. Discontinuous production system is worse than perfusion in terms of productivity.

SENSITIVITY



The variation of rhEPO cost is represented *versus* the variation of the market price of water, electricity and glucose in Thailand. Only operatinal costs are considered.

Water is the most influential factor in rhEPO operational cost:

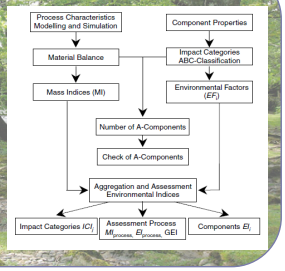
1. Medium preparation.
2. Culture broth dilution.

Electricity is the second more relevant consumable.

ENVIRONMENT

The General Environmental Index (GEI) determines quantitatively the ecological impact by considering all the inputs and outputs of the process.

The EF coefficient has been calculated by multiplication. In this case, the GEI rang is 1-256.
The GEI value of this bioprocess is **1.58: it's environmentally friendly.**



SOCIAL

Pharmaceutical product: positively accepted.
Political laws and taxes facilitate the start-up of a business.
Innovative capacity: employees are offered specific formation for their jobs.
Familiar and laboral timetables are compatibles: there are 3 shifts per day.

CONCLUSIONS

Taking into account the results above, this project is not viable economically. The main reason is the lack of coherence between the bibliographic sources used for defining the upstream and downstream process which results in a low purification yield. Consequently, it would be advisable to design another project using more consistent data (experimental adjustments of downstream are necessary) to obtain a more competitive process. The process is environmentally friendly so it is not necessary to change any component. Acetonitrile and ammonia are the most dangerous, but they be easily treated. The creation of jobs, a non-environmentally damaging process and well paid jobs result in the social acceptance of Epotech's new plant.

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